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EXAMINER
ROARK, JESSICA H

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/847,637	Applicant(s) NAPARSTEK ET AL.	
	Examiner Jessica H. Roark	Art Unit 1644	

-- The MAILING DATE of this communication appears n the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 October 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-27* is/are pending in the application.

4a) Of the above claim(s) *4,8-12,14 and 17-23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5-7,13,15,16,24,26 and 27* is/are rejected.

7)☒ Claim(s) *2,3 and 25* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *07 October 2002* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☒ The proposed drawing correction filed on *07 October 2002* is: a)☒ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *7* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Applicant's amendment, filed 10/7/02 (Paper No. 14), is acknowledged.
Claims 24-27 have been added.
Claims 1-3 have been amended.
Claims 1-27 *are pending.*

2. Applicant's election without traverse of Group I in Paper No. 14 is acknowledged.

Applicant's election with traverse of the species of SEQ ID NO:2 in Paper No. 14 is also acknowledged. The traversal is on the grounds that SEQ ID NOS: 2 and 3 are overlapping subfragments of SEQ ID NO:1 and thus a single search would suffice.

Although the search of even overlapping peptides is not necessarily co-extensive, in view of the rejection set forth below the search been extended to encompass each of SEQ ID NOS:1, 2 and 3.

Claims 4, 8-12, 14 and 17-23 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Claims 1-3, 5-7, 13, 15-16 and 24-27 *are under consideration in the instant application.*

Drawings

3. The proposed drawing corrections, filed on 10/7/02 have been approved.

However, the formal corrected drawings submitted fail to comply with 37 CFR 1.84.
Please see the enclosed form PTO-948.

Correction of Informalities -- 37 CFR 1.85
New corrected drawings must be filed with the changes incorporated therein. Identifying indicia, if provided, should include the title of the invention, inventor's name, and application number, or docket number (if any) if an application number has not been assigned to the application. If this information is provided, it must be placed on the front of each sheet and centered within the top margin. *The drawings should be filed as a separate paper with a transmittal letter addressed to the Official Draftsperson.*

Timing of Corrections
Applicant is required to submit acceptable corrected drawings within the time period set in the Office action. See 37 CFR 1.185(a). Failure to take corrective action within the set (or extended) period will result in ***ABANDONMENT*** *of the application.*

Priority

4. Provisional application 60/107,213 and PCT/IL99/00595 appear to provide adequate written support for instant claims 1-3, 5, 7, 13, 15-16 and 24-27.

However, the Examiner was unable to locate support for the limitation of instant claim 6 "a chemically modified peptide" in provisional application 60/107,213. Thus the filing date of claim 6 appears to be that of PCT/IL99/00595, i.e., 11/4/99.

Should the Applicant disagree with the Examiner's factual determination above, it is incumbent upon the Applicant to provide a showing that specifically supports the instant claim limitations.

IDS

5. Applicant's IDS, filed 12/17/01 and corrected on 2/14/02 (Paper Nos. 7 and 8), are acknowledged.

Applicant's filing on 2/14/02 of a supplemental PTO-1449 listing the same references as filed on 12/17/01 but correcting typographical errors and missing details is acknowledged. Only the corrected 1449, filed 2/14/02, has been initialed since the references listed are the same.

Specification

6. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention *to which the claims are directed.*

In addition, Applicant should avoid the use of novel in the title, as patents are presumed to be novel and unobvious.

It is suggested that Applicant amend the title to read -- B CELL EPITOPE PEPTIDES OF HSP65 --.

7. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which Applicant may become aware in the specification.

Claim Objections

8. Claim 16 is objected to because of the following informalities: it appears that the phrase "as claimed claim 15" should read -- as claimed in claim 15 --. Appropriate correction is required.

Claim Rejections - 35 USC § 112 first paragraph

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 1, 5-7, 13, 15-16, 24 and 26-27 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The following *written description* rejection is set forth herein.

The claims recite "a B cell epitope peptide comprising SEQ ID NOS:1, 2 or 3" as part of the invention.

The specification discloses SEQ ID NOS:2 and 3 which are overlapping sequences that define a peptide as set forth in SEQ ID NO:1. The specification also discloses that the peptides consisting of SEQ ID NOS:2 and 3 can be used to elicit an antibodies which bind the immunizing peptide and also the HSP 65 protein from which the peptides are derived (e.g., page 10 at lines 14-20). The specification also discloses that the peptides of SEQ ID NOS:2 and 3 of which SEQ ID NO:1 is comprised can be used as vaccines to suppress the development of arthritis in a rat model (e.g., Figure 4 and page 22).

However, there does not appear to be an adequate written description in the specification as-filed that the structure shared by SEQ ID NOS:1, 2 and 3 is sufficient in the context of additional amino acid sequence to elicit a protective antibody response. The Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement make clear that the written description requirement for a claimed genus may be satisfied by disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, see especially page 1106 3rd column).

In the instant case, although three species consisting of SEQ ID NO:1, 2 and 3 are disclosed, the comprising language of the instant claims creates an extremely large genus of peptides having the instantly recited amino acids of the three SEQ ID NOS, but also any number of additional undefined amino acids. Although these "peptides comprising" share a core structure, there does not appear to be disclosed a correlation between this core structure and the function of eliciting antibodies.

Consequently, Applicant was not in possession of the instant claimed invention. See Regents of the University of California v. Eli Lilly and Co. 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). Adequate written description of genetic material "'requires a precise definition, such as by structure, formula, chemical name, or physical properties,' not a mere wish or plan for obtaining the claimed chemical invention." Id. 43 USPQ2d at 1404 (quoting Fiers, 984 F.2d at 1171, 25 USPQ2d at 1606). The disclosure must allow one skilled in the art to visualize or recognize the identity of the subject matter of the claim. Id. 43 USPQ2d at 1406.

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Alternatively, Applicant is invited to point to clear support or specific examples of the claimed invention in the specification as-filed.

11. Claims 1, 5-7, 13, 15-16, 24 and 26-27 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for B cell epitope peptides consisting of SEQ ID NOS:1, 2 or 3 and vaccines comprising said peptides; does not reasonably provide enablement for B cell epitope peptides *comprising* SEQ ID NOS:1, 2 or 3, or for vaccines comprising. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification discloses SEQ ID NOS:2 and 3 which are overlapping sequences that define a peptide as set forth in SEQ ID NO:1. The specification also discloses that the peptides consisting of SEQ ID NOS:2 and 3 can be used to elicit an antibodies which bind not only the immunizing peptide, but also the HSP 65 protein from which the peptides are derived (e.g., page 10 at lines 14-20). The specification also discloses that the peptides of SEQ ID NOS:2 and 3 of which SEQ ID NO:1 is comprised can be used as vaccines to suppress the development of arthritis in a rat model (e.g., Figure 4 and page 22).

However, there is insufficient guidance and direction to permit the skilled artisan to make and use B cell epitope peptides *comprising* SEQ ID NOS:1, 2 or 3, or vaccines comprising said peptides, as broadly claimed.

The scope of the instant claims encompasses peptides, and vaccines comprising said peptides, in which the peptides have highly diverse amino acid sequences, so long as within that sequence is a stretch of amino acids comprising SEQ ID NO:1, 2 or 3. However, the specification does not appear to provide sufficient guidance as to what additional amino acid residues could "flank" the peptides consisting of SEQ ID NO:1, 2 or 3 without ablating the ability of the peptide to elicit antibody to the peptide which also binds HSP65. Neither does the specification appear to provide sufficient guidance as to the number of "flanking" amino acid residues that may be added to the sequences set forth in SEQ ID NOS:1, 2 or 3 without ablating the ability of the peptide to elicit antibody to the peptide which also binds HSP65. The specification does not appear to provide working examples that a peptide comprising SEQ ID NO:1, 2 or 3 in the context of a larger peptide sequence would still generate the requisite antibody epitope.

Lederman et al. (Molecular Immunology 1991; 28: 1171-1181) teach that a single amino acid substitution in a common allele ablates binding of a monoclonal antibody (see entire document). Similarly, Li et al. (PNAS 1980; 77: 3211-3214) teach that dissociation of immunoreactivity from other biological activities occurs when constructing analogs (see entire document). In some cases alteration of residues not part of the amino acid sequence actually bound by an antibody (the also affect binding (see Van Regenmortel *Methods: A Companion to Methods of Enzymology* 1996; 9:465-472, see page 469, column 1 in particular). Thus it is unpredictable which amino acid residues could be added to a peptide and yet still result in a peptide that would elicit an antibody that bound the peptide and HSP65 and would therefore function as a vaccine.

Thus the scope of the instant claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of peptides of undefined "flanking" sequences broadly encompassed by the instant claims. The scope of the claims must bear a reasonable correlation with the scope of enablement. See In re Fisher, 166 USPQ 19 24 (CCPA 1970).

Without sufficient guidance, it is unpredictable as to the identity and number of additional amino acid residues that could be added to the peptides of SEQ ID NOS:1, 2 or 3 and still result in a peptide that would elicit an antibody that bound both the peptide and HSP65, and could therefore be used in a vaccine composition as disclosed. Consequently, the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue.

Claim Rejections – 35 U.S.C. § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

13. Claims 1, 5-7, 13, 15-16, 24 and 26-27 are rejected under 35 U.S.C. 102(e) as being anticipated by Tan et al. (U.S. Pat. No. 5,985,287, see entire document), as evidenced by the attached alignments.

Tan et al. teach polypeptides from the mycobacterium *M. vaccae* (see entire document). Tan et al. teach the *M. vaccae* 65kD heat shock protein (clone GV-27) set forth in SEQ ID NO:114 (see sequence listing and columns 28-29). Tan et al. also teach the a peptide fragment of GV-27 (GV-27A) which is an N-terminal sequence (see SEQ ID NO:114 and column 29, especially lines 26-33).

As evidenced by the attached alignment, SEQ ID NO:114 of Tan et al. is a peptide comprising each of instant SEQ ID NO:1, SEQ ID NO:2 and SEQ ID NO:3.

Since instant SEQ ID NO:1, SEQ ID NO:2 and SEQ ID NO:3 are contained within the peptide sequence set forth in SEQ ID NO:114 of Tan et al., this peptide is inherently a "B cell epitope peptide".

Tan et al. teach that the *M. vaccae* polypeptides and portions thereof can be produced by either recombinant or synthetic techniques (see columns 8-9, especially column 8 at lines 49-63).

Chemical modification of the *M. vaccae* polypeptides is taught at columns 12-13. For example, the coupling of the polypeptide to a solid support via either a direct linkage or a cross-linking agent involves a chemical modification of the polypeptide (e.g., column 12 at lines 60-66).

Tan et al. also teach that the *M. vaccae* polypeptides and portions thereof can be used as vaccines comprising pharmaceutically acceptable carriers and other diluents and additives, including adjuvants (see columns 4, 10-12 and 37-38 which describe vaccine formulations, including the peptide of SEQ ID NO:117, and that the *M. vaccae* polypeptides and portions thereof, including the GV-27 polypeptide, stimulate IL-12 production). Although Tan et al. do not explicitly state that the vaccine confers immunity against autoimmune or inflammatory disorders, including arthritis, these properties are inherent in a vaccine comprising the *M. vaccae* polypeptide of SEQ ID NO:117.

Applicant is reminded that the intended uses stated with respect to the vaccines comprising do not carry patentable weight per se and the claims read on the active or essential ingredients of the compositions. For example in Atlas Powder Co. V. IRECO, 51 USPQ2d 1943 (Fed. Cir. 1999); the following was noted. "Artisans of ordinary skill may not recognize the inherent characteristics or functioning of the prior art. However, the discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." The Court further held that "this same reasoning holds true when it is not a property but an ingredient which is inherently contained in the prior art."

No more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations would be inherent properties of the polypeptide of SEQ ID NO:117 of Tan et al. or said polypeptide formulated as a vaccine composition. A composition is a composition irrespective of what its intended use is.

The reference teachings thus anticipate the instant claimed invention.

Conclusion

14. No claim is allowed.

15. Claims 2-3 and 25 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jessica Roark, whose telephone number is (703) 605-1209. The examiner can normally be reached Monday to Friday from 8:00 to 4:30. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Jessica Roark, Ph.D.
Patent Examiner
Technology Center 1600
December 20, 2002

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